MAYO CLINIC

Pharmacotherapeutic Failure in a Large Cohort of Patients With Insomnia Presenting to a Sleep Medicine Center and Laboratory: Subjective Pretest Predictions and Objective Diagnoses

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Abstract

Objective: To measure the frequency of pharmacotherapeutic failure and its association with the diagnosis of sleep-disordered breathing among patients with chronic insomnia disorder.

Patients and Methods: In a retrospective review of medical records from January 1, 2005, through December 31, 2012, we identified an inclusive, consecutive series of 1210 patients with insomnia disorder, 899 (74.3%) of whom used sleep aids either occasionally (168 [18.7%]) or regularly (731 [81.3%]). Patients presented to a community-based sleep medicine center in Albuquerque, New Mexico, with typical referral patterns: 743 (61.4%) were referred by primary care physicians, 211 (17.4%) by specialists, 117 (9.7%) by mental health professionals, and 139 (11.5%) by self-referral. Pharmacotherapeutic failure was assessed from subjective insomnia reports and a validated insomnia severity scale. Polysomnography with pressure transducer (an advanced respiratory technology not previously used in a large cohort of patients with insomnia) measured sleep-disordered breathing. Objective data yielded accuracy rates for 3 pretest screening tools used to measure risk for sleep-disordered breathing.

Results: Of the total sample of 1210 patients, all 899 (74.3%) who were taking over-the-counter or prescription sleep aids had pharmacotherapeutic failure. The 710 patients taking prescription drugs (79.0%) reported the most severe insomnia, the fewest sleep-associated breathing symptoms, and the most medical and psychiatric comorbidity. Of the 942 patients objectively tested (77.9%), 860 (91.3%) met standard criteria, on average, for a moderate to severe sleep-associated breathing disorder, yet pretest screening sensitivity for sleep-disordered breathing varied widely from 63.7% to 100%. Positive predictive values were high (about 90%) for all screens, but a tool commonly used in primary care misclassified 301 patients (32.0% false-negative results).

Conclusion: Pharmacotherapeutic failure and sleep-disordered breathing were extremely common among treatment-seeking patients with chronic insomnia disorder. Screening techniques designed from the field of sleep medicine predicted high rates for sleep-disordered breathing, whereas a survey common to primary care yielded many false-negative results. Although the relationship between insomnia and sleep-disordered breathing remains undefined, this research raises salient clinical questions about the management of insomnia in primary care before sleep center encounters.

 ■ Mayo Clin Proc. 2014;89(12):1608-1620

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Insomnia is the most common sleep complaint and affects millions of adults.[1,2] Chronic insomnia is linked to daytime impairment,[2] disability,[3] motor vehicle crashes,[4] workplace absenteeism[5] and errors,[4] and excess medical service utilization.[3] It also aggravates or increases risk for alcoholism,[6] depression,[7] diabetes,[8] obesity,[9] and stroke.[10] The economic burden of insomnia has been calculated in the tens of billions of dollars.[11,12]

Although insomnia is encountered routinely in the primary care setting,[1,2,13] it often goes undiagnosed or untreated for years.[14,15] Disregard for insomnia concerns may be a function of physician training or knowledge[16-18]; conversely, patients may avoid discussing insomnia with their doctors or may not envision useful treatments for this sleep disorder.[19,20] The apparent lack of attention to insomnia care may occur as a result of a vast medical literature that defines insomnia as a symptom, secondary to a primary disorder (eg, cancer or depression). When the primary condition is treated, insomnia presumably resolves.[21]

Mayo Clin Proc. ■ December 2014;89(12):1608-1620 ■ http://dx.doi.org/10.1016/j.mayocp.2014.04.032
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In primary care clinics, treatment offered for insomnia usually consists of 3 approaches: basic sleep hygiene education,[22] over-the-counter (OTC) sleep aids, or sedatives/hypnotics and other sedating medications by prescription.[2,13,23,24] Although no definitive epidemiological studies on the application of sleep education or prescription of sleep aids by primary care physicians are available,[15] Centers for Disease Control and Prevention and National Health and Nutrition Examination Survey studies report that sedative prescriptions are increasing.[25,26] Notwithstanding, protracted use of prescription sedating medications (both indicated and off-label use) is a controversial subject.[27] Unquestionably, prescription sedatives help some patients with insomnia in the primary care setting,[28,29] including some who use these medications nightly for several months[30] or potentially longer.[31,32] Clinical trials often report minimal complications[31,33] among a large proportion of sedative users, including long-term users, although it is not always as clear whether these patients are achieving optimal outcomes.[29] Counter to these observations, some reviews report that sedatives are of limited[34] or no[35] efficacy for most patients with chronic insomnia. Conventional wisdom suggests that sedatives may be used frequently for short periods and then discontinued for myriad reasons. Lastly, emerging research has raised questions about increased risks for mortality,[36,37] suicidality,[38] and other adverse effects[39] associated with sedatives. Still, prescription sedatives for chronic insomnia represent only one form of treatment—a symptomatic therapy that may not lead to remission or cure when drug use ceases; thus, if this form of therapy fails to resolve episodes of sleeplessness, it is unclear how primary care physicians proceed with these patients.[16,40]

In contrast to primary care experiences, newer perspectives and guidelines from the fields of sleep medicine[41] and psychiatry[42] view insomnia as a comorbid disorder rather than a symptom, which then warrants independent clinical assessment and treatment. This point is key to the specialty of sleep medicine, whose main imperative is to determine whether the patient with chronic insomnia is receiving an efficacious treatment,[24] which often leads to an assessment of whether pharmacotherapy is yielding optimal results. When pharmacotherapy is failing, it requires a more thorough sleep medicine evaluation and usually a broader array of therapeutic options.[16,24] In particular, pharmacotherapeutic failure raises suspicions for additional complex physiologic etiologies for sleeplessness,[24] a direct indication for polysomnography (PSG) per American Academy of Sleep Medicine (AASM) guidelines.[24,43] Of potential clinical importance, recent research focusing on PSG diagnostics revealed surprisingly high rates of the physiologic disorder sleep-disordered breathing (SDB) among patients with insomnia[44-49]—referred to as *complex insomnia*.[50] Two studies revealed very high rates of obstructive sleep apnea (OSA) or upper airway resistance syndrome (UARS)[51,52] in hypnotic-dependent patients with insomnia who were seeking treatment at a sleep medicine center specifically for the chief complaint of persistent insomnia symptoms despite sedating medication use.

This combination of sleep disorders—insomnia and SDB—creates clinical confusion, not only because each one causes sleep fragmentation effects but also because both disorders present with overlapping symptoms such as nonrestorative sleep, awakenings at night, and difficulty returning to sleep.[53,54] This comorbidity may further complicate physicians' efforts to assess pharmacotherapeutic efficacy because of their lack of familiarity with the intricacies and assessments of either or both sleep disorders. In theory, confusion arises when primary care physicians face the challenge of prescribing different drugs or revising dosages to treat residual insomnia symptoms[16] instead of considering potential comorbid SDB and referral to a sleep center.[23] Identifying pharmacotherapeutic failure may also be obscured if drug efficacy estimates are based on limited knowledge[22] or influenced by vested interests.[55] Making matters worse, no formal standards have been published to define pharmacotherapeutic failure for insomnia drugs.[24]

When pharmacotherapeutic failure is suspected in primary care settings, many factors may dissuade physicians from referring patients with insomnia to sleep medicine centers for sleep specialist consultations or to sleep medicine laboratories for overnight testing. However, when primary care physicians suspect sleep apnea in a patient with insomnia,